A ONE-PAGE SCIENTIFIC ABSTRACT OF THE PROTOCOL:

We propose a protocol to transduce human bone marrow cells with the multiple drug resistance (MDR) gene. This is done to increase the expression of MDR in human bone marrow cells that usually express very low levels of this important glycoprotein. High MDR-producing marrow cells are necessary to prevent killing of these cells with several classes of chemotherapeutic agents, including taxol, anthracyclines, vinca-alkaloids, and etoposides. Usually, when high doses of chemotherapeutic agents including those mentioned above are employed, significant bone marrow toxicity is induced. To avoid this toxicity, autologous bone marrow transplantation (ABMT) (the removal of human bone marrow and its reinfusion) is done in association with the administration of high-dose chemotherapy for patients with advanced cancer.

The transduction of the removed bone marrow cells by a retrovirus containing the MDR gene is proposed. These transduced cells will be reinfused into patients as is ordinarily done in ABMT with high-dose chemotherapy. It is hoped that the expression of MDR in the transduced bone marrow cells will induce resistance of these cells to the toxic effects of subsequent chemotherapy. A safe and efficient line of cells producing a retrovirus efficient in transferring the MDR gene into animal bone marrow cells will be used in this study and is expected to have no toxicity. The potential benefit of the protocol is that it may create a population of human bone marrow cells resistant to the toxicity of high-dose chemotherapy with drugs such as taxol, an MDR-responsive agent in patients with advanced breast and ovarian cancers, and either allow these patients to receive higher doses of taxol or allow patients to be treated with taxol who could not tolerate this therapy because of its bone marrow toxicity. If this treatment is successful, it could be used to administer higher dose chemotherapy to patients undergoing ABMT at earlier times and increase the possibility of prolonged survival or cure in these patients.

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